

REMARKS

Status of the Claims

Claims 1-6 and 8-21 are pending. Claims 1 and 2 have been amended. Claims 10 and 13-19 are withdrawn from consideration.

No New Matter Has Been Added

Applicants submit that no new matter has been added by way of the present amendment. For instance, claim 1 has been amended to replace the recitation of "mutated" with "substituted". Also, the functional language has been removed from claim 1. Lastly, a specific sequence, SEQ ID NO:4, has been added to claim 2. Accordingly, no new matter has been added.

In view of the following remarks, Applicants respectfully request that the Examiner withdraw all rejections and allow the currently pending claims.

Issues Under 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 1-9, 11-12 and 20-21 under 35 U.S.C. § 112, second paragraph for the reasons recited at page 4 of the outstanding Office Action. Applicants respectfully traverse these rejections.

First, the Examiner has rejected claim 1 asserting that the term "mutated" is indefinite. Applicants traverse and submit that this language has been changed to "substituted", a term well known in the art. Accordingly, there no longer exists any issue with respect to the indefiniteness of claim 1.

Second, the Examiner has rejected claim 2 asserting that the recitation of a specific sequence is required. Applicants have referred to SEQ ID NO:4 to provide a reference point. Accordingly, this rejection is moot.

In view of the above, Applicants submit that the present claims define fully definite subject matter. Reconsideration and withdrawal of the above rejections are requested.

Issues Under 35 U.S.C. § 103(a)

The Examiner has rejected claims 1-6 and 8 under 35 U.S.C. §103(a) as being obvious over Thastrup et al., WO 97/11094 (hereinafter referred to as Thastrup) in view of Ehrig et al., FEBS Letters, Vol. 367, pages 163-166, 1995 (hereinafter referred to as Ehrig). Applicants respectfully traverse this rejection.

The Examiner asserts that the Thastrup article discloses the F64L mutation of GFP and the Ehrig reference discloses the E222G mutation of GFP. Applicants disagree with the Examiner's combination and reading of the cited art.

The present claims involve a combination of the F64L and E222G mutations of GFP. As described in the present specification, the F64L,E222G-GFP has an excitation maximum of 470 nm and an emission maximum of 505 nm (see Figure 3, and example 2 of the present specification).

In contrast, the GFP mutant described by Ehrig has an excitation maximum of 481nm and an emission maximum at 506nm (page 2, lines 14-16 of the present specification). It is clear from the Thastrup reference, that the F64L mutation only alters the folding kinetics of GFP, not the spectral properties (see section starting on page 3, line 30 to page 4, line 6, and examples of the present application). Thus, the skilled person would have no idea that a combination of Thastrup and Ehrig, as proposed by Examiner, would result in a GFP product with this increased Stokes-shift. A Stokes shift of 35 nm for F64L,E222G-GFP results in a significant increase in the excitation-emission band separation for F64L,E222G-GFP with several implications for the use of F64L,E222G-GFP in high-throughput screening (see page 5, lines 1-15 of the present specification).

In summary, Applicants submit that even if it were hypothetically established that one of skill in the art would have been motivated to combine Thastrup with Ehrig as suggested by the Examiner, a point not conceded by Applicants, it is

submitted that there is no suggestion of the unexpected and superior results achieved by the present invention. That is, there could have been no expectation of the increased Stokes shift of 35 nm for the presently claimed subject matter compared to the prior art. Thus, these unexpected and superior results rebut any hypothetical *prima facie* case of obviousness.

Accordingly, the disclosures of Thastrup and Ehrig, whether taken alone or in combination, fail to suggest or disclose the presently claimed subject matter, much less the unexpected results according to the present invention. Therefore, the Examiner is respectfully requested to withdraw all rejections and allow the currently pending claims.

If the Examiner has any questions or comments, please contact Craig A. McRobbie, Reg. No. 42,874, at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees

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required under 37 C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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